

Application No.: 09/602,688  
Applicant: Lai and Wang  
Filed: June 23, 2000  
9

PATENT  
Attorney Docket No.: MEDIN1400  
(023161-2401)

APPENDIX

1. (Amended) A compound having the structure:

X-L-Z

wherein:

X = a non-steroidal anti-inflammatory drug (NSAID),

L = a[n optional] covalent bond, a linker[/], or a spacer,

Z = a sulfur-containing functional group containing a[n optionally] substituted or unsubstituted hydrocarbyl moiety, wherein the sulfur-containing functional group is sulfoxide, sulfonate, reverse sulfonate, sulfonamide, reverse sulfonamide, sulfone, sulfinate, or reverse sulfinate.

2. (Reiterated) A compound according to claim 1 wherein said NSAID is acetaminophen, aspirin, ibuprofen, choline magnesium salicylate, choline salicylate, diclofenac, diflunisal, etodolac, fenpropfen calcium, flurobiprofen, indomethacin, ketoprofen, carprofen, indoprofen, ketorolac tromethamine, magnesium salicylate, meclofenamate sodium, mefenamic acid, oxaprozin, piroxicam, sodium salicylate, sulindac, tolmetin, meloxicam, nabumetone, naproxen, lornoxicam, nimesulide, indoprofen, remifenzone, salsalate, tiaprofenic acid, or flosulide.

3. (Amended) A compound according to claim 2 wherein said NSAID is diclofenac, naproxen, aspirin, ibuprofen, flurbiprofen, indomethacin, ketoprofen, or carprofen.

5. (Amended) A compound according to claim [4] 1 wherein the sulfur-containing functional group is sulfonate or reverse sulfonate.

A

Application No.: 09/602,688

Applicant: Lai and Wang

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10

PATENT

Attorney Docket No.: MEDIN1400

(023161-2401)

6. (Amended) A compound according to claim 5 wherein the sulfur-containing functional group is a[n optionally] substituted or unsubstituted aromatic sulfonate.
7. (Reiterated) A compound according to claim 6 wherein said aromatic sulfonate is tosylate or brosylate.
8. (Amended) A compound according to claim 5 wherein the sulfur-containing functional group is a[n optionally] substituted or unsubstituted C1 to C10 alkyl sulfonate.
9. (Reiterated) A compound according to claim 8 wherein the alkyl sulfonate is mesylate or triflate.
10. (Amended) A compound according to claim [4] 1 wherein the sulfur-containing functional group is a sulfone.
11. (Amended) A compound according to claim 10 wherein the sulfur-containing functional group is a[n optionally] substituted or unsubstituted C1 to C10 alkyl sulfone.
12. (Reiterated) A compound according to claim 11 wherein said sulfone is methyl sulfone, ethyl sulfone.
13. (Amended) A compound according to claim 10 wherein the sulfur-containing functional group is a[n optionally] substituted or unsubstituted aromatic sulfone.
14. (Reiterated) A compound according to claim 13 wherein the sulfur-containing functional group is a p-substituted aromatic sulfone.
15. (Amended) A compound according to claim [4] 1 wherein the sulfur-containing functional group is a sulfonamide or reverse sulfonamide.

A

Application No.: 09/602,688  
Applicant: Lai and Wang  
Filed: June 23, 2000  
11

PATENT  
Attorney Docket No.: MEDIN1400  
(023161-2401)

16. (Amended) A compound according to claim 15 wherein the sulfur-containing functional group is a[n optionally] substituted or unsubstituted C1 to C10 alkyl sulfonamide.

17. (Reiterated) A compound according to claim 16 wherein the sulfur-containing functional group is methyl sulfonamide.

18. (Amended) A compound according to claim 15 wherein the sulfur-containing functional group is a[n optionally] substituted or unsubstituted aromatic sulfonamide.

19. (Reiterated) A compound according to claim 18 wherein the sulfur-containing functional group is toluene sulfonamide.

20. (Amended) A compound according to claim [4] 1 wherein the sulfur-containing functional group is a sulfinic acid or reverse sulfinic acid.

21. (Amended) A compound according to claim 1 wherein L[, when present,] has the structure:

-W-R-

wherein:

R is [optional] present or absent, and when present is alkylene, substituted alkylene, cycloalkylene, substituted cycloalkylene, heterocyclic, substituted heterocyclic, oxyalkylene, substituted oxyalkylene, alkenylene, substituted alkenylene, arylene, substituted arylene, alkarylene, substituted alkarylene, aralkylene or substituted aralkylene, and

W is ester, reverse ester, thioester, reverse thioester, amide, reverse amide, phosphate, phosphonate, imine or enamine.

22. (Reiterated) A formulation comprising a compound according to claim 1 in a pharmaceutically acceptable carrier therefor.

A

Application No.: 09/602,688  
Applicant: Lai and Wang  
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12

PATENT  
Attorney Docket No.: MEDIN1400  
(023161-2401)

23. (Reiterated) A formulation according to claim 22 wherein said pharmaceutically acceptable carrier is a solid, solution, emulsion, dispersion, micelle or liposome.

24. (Reiterated) A formulation according to claim 22 wherein said pharmaceutically acceptable carrier further comprises an enteric coating.

25. (Amended) In a method for the administration of a non-steroidal anti-inflammatory drug (NSAID) to a subject for the treatment of a pathological condition, the improvement comprising directly or indirectly covalently attaching said NSAID to a sulfur-containing functional group containing a[n optionally] substituted or unsubstituted hydrocarbyl moiety prior to administration thereof to said subject.

26. (Reiterated) The method of claim 25 wherein said pathological condition is septic shock, hemorrhagic shock, anaphylactic shock, toxic shock syndrome, ischemia, cerebral ischemia, administration of cytokines, overexpression of cytokines, ulcers, inflammatory bowel disease, diabetes, arthritis, asthma, Alzheimer's disease, Parkinson's disease, multiple sclerosis, cirrhosis, allograft rejection, encephalomyelitis, meningitis, pancreatitis, peritonitis, vasculitis, lymphocytic choriomeningitis, glomerulonephritis, uveitis, ileitis, inflammation, burn, infection, hemodialysis, chronic fatigue syndrome, stroke, cancers, cardiopulmonary bypass, ischemic/reperfusion injury, gastritis, adult respiratory distress syndrome, cachexia, myocarditis, autoimmune disorders, eczema, psoriasis, heart failure, heart disease, atherosclerosis, dermatitis, urticaria, systemic lupus erythematosus, AIDS, AIDS dementia, chronic neurodegenerative disease, chronic pain, priapism, cystic fibrosis, amyotrophic lateral sclerosis, schizophrenia, depression, premenstrual syndrome, anxiety, addiction, migraine, Huntington's disease, epilepsy, neurodegenerative disorders, gastrointestinal motility disorders, obesity, hyperphagia, solid tumors, malaria, hematologic cancers, myelofibrosis, lung injury, graftversushost disease, head injury, CNS trauma, hepatitis, renal failure, liver disease, druginduced lung injury, myasthenia gravis (MG), ophthalmic diseases, postangioplasty, restenosis, angina, or coronary artery disease.

A

Application No.: 09/602,688  
Applicant: Lai and Wang  
Filed: June 23, 2000  
13

PATENT  
Attorney Docket No.: MEDIN1400  
(023161-2401)

27. (Amended) In the treatment of a subject suffering from a pathological condition by administration thereto of a non-steroidal anti-inflammatory drug (NSAID), the improvement comprising covalently attaching said NSAID to a sulfur-containing functional group containing a[n optionally] substituted or unsubstituted hydrocarbyl moiety prior to administration thereof to said subject.

28. (Amended) A method for the treatment of a subject afflicted with a pathological condition, said method comprising administering to said subject an effective amount of a non-steroidal anti-inflammatory drug (NSAID),

wherein said NSAID is effective for treatment of said condition, and

wherein said NSAID has been modified by the direct or indirect covalent attachment thereto of a sulfur-containing functional group containing a[n optionally] substituted or unsubstituted hydrocarbyl moiety.

29. (Amended) A method for the preparation of a protected form of a non-steroidal anti-inflammatory drug (NSAID), said method comprising directly or indirectly covalently attaching a sulfur-containing functional group containing a[n optionally] substituted or unsubstituted hydrocarbyl moiety to said NSAID.

30. (Reiterated) A method according to claim 29 wherein said NSAID is acetaminophen, aspirin, ibuprofen, choline magnesium salicylate, choline salicylate, diclofenac, diflunisal, etodolac, fenpropfen calcium, flurbiprofen, indomethacin, ketoprofen, carprofen, indoprofen, ketorolac tromethamine, magnesium salicylate, meclofenamate sodium, mefenamic acid, oxaprozin, piroxicam, sodium salicylate, sulindac, tolmetin, meloxicam, nabumetone, naproxen, lornoxicam, nimesulide, indoprofen, remifentanyl, salsalate, tiaprofenic acid, or flosulide.

31. (Amended) A method for reducing the side effects induced by administration of a non-steroidal anti-inflammatory drug (NSAID) to a subject, said method comprising directly or indirectly covalently attaching a sulfur-containing functional group containing a[n optionally]

A

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Filed: June 23, 2000  
14

PATENT  
Attorney Docket No.: MEDIN1400  
(023161-2401)

substituted or unsubstituted hydrocarbyl moiety to said NSAID prior to administration to said subject.

32. (Amended) A method for enhancing the effectiveness of a non-steroidal anti-inflammatory drug (NSAID), said method comprising directly or indirectly covalently attaching a sulfur-containing functional group containing a[n optionally] substituted or unsubstituted hydrocarbyl moiety to said NSAID.

33. (Reiterated) A method for the prevention or treatment of an inflammatory or infectious disease in a subject in need thereof, said method comprising administering to said subject an amount of the compound of claim 1 effective to alleviate said condition.

34. (New) A compound according to claim 1 wherein the sulfur-containing functional group is sulfoxide.

A